

### **REMARKS/ARGUMENTS**

The Official Action dated February 24, 2005 has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

#### **35 USC §112, First Paragraph**

The Examiner has objected to claims 1 and 3-7 under 35 USC §112, first paragraph, as lacking enablement for any antidepressant-induced mania induced by any antidepressant. The Examiner confirms that the specification is enabling for determining the susceptibility of Bipolar I or Bipolar II patients to antidepressant-induced mania related to Bipolar Disorder, wherein the antidepressant is a pro-serotonergic agent. We respectfully submit that the specification does enable the full scope of the claims for the reasons that follow.

The present invention relates to a method and determining whether or not a patient is susceptible to antidepressant-induced mania. Specifically, the method comprises testing a sample from the patient for the presence of the s variant of the 5HTTLPR polymorphism in the 5HTT gene which would indicate that the patient is susceptible to antidepressant-induced mania.

Antidepressant-induced mania is a phenomenon that can be observed in any patient on antidepressants. Such patients include people with a Bipolar Disorder, a major depressive disorder or obsessive-compulsive disorder. In this regard, we enclose a review article by Chun & Dunner (Bipolar Disorders, 2004: 6:32-42) that demonstrates that mania can be induced by antidepressants in patients with major depression. The review article also demonstrates that this phenomenon can be observed in many classes of antidepressants and it is not just limited to the serotonergic agents. In this regard, we refer to Table 4 of the paper.

Antidepressant-induced mania has also been observed in patients with obsessive-compulsive disorder. In this regard, we enclose a copy of a letter to the Editor by Diaferia et. al. that appeared in the Journal of Clinical Psychopharmacology in February, 1994. We also include a letter to the Editor by Vieta and Bernardo that appeared in the American Journal of Psychiatry in September 1992. We further include a letter to the Editor by Mundo et. al. that appeared in Hospital and Community Psychiatry in July, 1993. Therefore, the attached references demonstrate that the antidepressant-induced mania can be observed in different patients and can be caused by various types of antidepressants.

In making the objection, the Examiner references several passages in the "Background of the Invention" section of the present application. While the background may suggest that the induction of mania occurs more frequently in patients with Bipolar Disorder, it does clearly specify that the induction of mania can occur in patients with other disorders as evidenced by many of the papers cited in the reference section on pages 18-23. However, regardless of the frequency of antidepressant-induced mania that occurs within a specific population, the scope of the claims is still enabled as it allows one of skill in the art to determine whether or not a particular patient will be susceptible to antidepressant-induced mania.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC§112, first paragraph be withdrawn.

**35 USC§102(b)**

The Examiner has objected to claims 1-5 under 35 USC§102(b) as being anticipated by Mundo et. al. (abstract in Biological Psychiatry, 2000, 47(suppl):135S). We respectfully disagree with the Examiner for the reasons that follow.

Mundo et. al. is an inventor derived publication that was published on April 15, 2000. In support of the publication date, we enclose a copy of a search that indicates the publication date of April 15, 2000. The Mundo et. al. abstract as presented at the 55<sup>th</sup> Annual Convention of the Society of Biological Psychiatry which was held in Chicago on May 11-13, 2000. The priority date of the application is February 16, 2001. As a result, the Mundo et. al. abstract was published less than one year prior to the priority date of the present application.

We are enclosing a declaration under 37 CFR 1.132 of inventor James Kennedy that provides evidence that three of the co-authors on the abstract, M. Walker, H. Tims and F.M. Macciardi are not inventors of the present application.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC§102(b) be withdrawn.

**35 USC§103(a)**

The Examiner has objected to claims 1-7 under 35 USC§103(a) as being unpatentable over Williams et. al. (US Patent App. No. 10/625,134) in view of Bellivier et. al. (Neuroscience Letters, 1998, 255:143-46) and Mundo et. al. (abstract in Biological Psychiatry, 2000, 47(suppl):135S).

Williams is concerned with determining the susceptibility of patients to disease or stress. Notably, at paragraph 0042, Williams specifically excludes "mental or psychiatric disease" from the definition of "disease". Williams et. al. does not disclose or even remotely suggest that detecting the s variant of the 5HTTLPR polymorphism in the 5HTT gene is indicative of antidepressant-induced mania. Further, Williams et. al. teaches away from the present invention as it directs the skilled artisan away from testing patients with diseases that may be mental or psychiatric.

The deficiencies in Williams et. al. are in no way remedied by Bellivier et. al. or Mundo et. al. either alone or in combination. As mentioned above, Mundo et. al. is not citable against the present invention as it is an inventor-derived publication that occurred less than one year prior to the present priority date. Bellivier et al. is not relevant as it relates to the role of a serotonin-transported gene in Bipolar Disorder but does not mention or remotely suggest the role of the gene in antidepressant-induced mania.


In view of the foregoing, we respectfully request that the objections to the claims under 35 USC§103(a) be withdrawn.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication of that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, she is kindly requested to contact the undersigned by telephone at (416) 957-1682 at her convenience.

Respectfully submitted,

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Attachments